## REMARKS

Applicants respectfully traverse the new matter rejections with respect to the amendments to the specification. In particular, Applicants note that there is no rule against deleting incorporations by reference. Thus, it is within the volition of the Applicants whether the incorporation by reference of other patents and applications should be included or not within the application. As such, it is never "new matter" to delete such incorporations. Moreover, Applicants respectfully submit that it is also their absolute right to correct inconsistencies or misstatements in the application. In that regard, Applicants are not correcting "admissions" with respect to correcting these misstatements.

This is not an issued patent but instead is a pending application. Applicants respectfully point out that there is no "law of admissions" that bars the correction of misstatements during the prosecution process. Applicants readily admit that the doctrine of prosecution history estoppel holds a patentee to certain statements or "admissions." For example, if during prosecution, the patentee admits that his claims do not include "x" within their scope, that admission will stick should the patentee later try to assert that his claim scope includes "x."

But that is clearly not the case here: this is a pending application. Applicants' claims are not set in stone yet. Applicants have identified statements within the specification that are clearly at variance with the disclosed invention. Accordingly, it is Applicants' right to delete these statements. To better illustrate the issue, consider what is it is that Applicants have invented and disclosed. For example, Applicants have significantly advanced the state of the art with respect to mass spectrometry metrology. Through the use of atmospheric pressure ionization, intelligent spiking, and ratio measurements, a truly automated and stand alone mass spectrometer is provided. Whereas conventional mass spectrometry metrology typically requires significant hands on monitoring by highly-trained personnel, Applicants provide a mass spectrometer that needs no human intervention or monitoring over many measurement cycles. For the first time, quanititative mass spectrometry may be used in applications such as semiconductor clean rooms.

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An overview of this innovation is shown in Figure 2. A controller (element 217) controls a "sample introduction apparatus" (element 203) to draw an appropriate amount of sample, which is then spiked by "spike introduction apparatus" (element 205). After equilibration of the spiked sample, it is ionized in "atmospheric ion generator" (element 211) and the mass/charge distributions of the resulting ions measured in mass spectrometer 213. The controller may then determine the concentration of an analyte in the sample using a ratio measurement of certain mass/charge peaks in the spectrum.

Applicants readily admit that this ratio measurement may be an isotopic ratio as used in an isotope dilution mass spectrometry (IDMS) technique. However, as stated by the Applicants on page 35, the invention includes numerous other embodiments that do not use the IDMS technique. For example, as stated on lines 8 – 11 of that page: "in some cases addition of standard concentrations of monoisotopic elements, that is, elements that do not exhibit a plurality of isotopes in the natural state, may be used in many procedures." For this reason, Applicants noted that their apparatus may be used to analyze for concentrations of Co and Mn on page 21, lines 4 through 10, both of which are virtually monoisotopic such that IDMS techniques cannot be used: there is no naturally-occurring isotopic ratio to alter for such elements.

A ratio measurement not using IDMS would involve the well-known internal standard technique. In that technique, the sample is spiked with a known concentration of an internal standard that chemically behaves sufficiently similar to the analyte of interest in the sample such that by comparing the mass/charge response for the analyte to the mass/charge response for the internal standard, the concentration of the analyte may be determined.

Regardless of the type of ratio being used, the beauty of this invention is that instrument drift and other inaccuracies are naturally cancelled by the ratio measurement. Furthermore, the use of atmospheric pressure ionization (API) preserves chemical species information as compared to traditional IDMS techniques involving the use of inductively coupled plasma. Unlike the relatively harsh ionization used in traditional inductively-coupled plasma mass spectrometers , API provides a more mild ionization that preserves species information. For example, should the species Cr(III) and Cr(VI) be ionized in an inductively-coupled plasma MS instrument, they are ionized into the same state, namely

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Cr(I). A MS cannot distinguish between a Cr(I) ion that was originally Cr(III) vs. a Cr(I) ion that was originally Cr(VI). So, the species information is destroyed. However, the relatively mild ionization provided by an API ionization process would not convert Cr(III) and Cr(VI) into the same ionic form. For example, suppose a sample contains $CrF_3$ and $CrF_6$. When subjected to API, such a sample will provide $(CrF_2)+$ ions and $(CrF_5)+$ ions, thereby preserving the Cr(III) and Cr(VI) species information.

Moreover, the implementation of an API ionization stage is only one feature of Applicants' invention. For example, consider the dilution module described with respect to Figure 6. As described, for example, beginning at page 30, line 19, this dilution module may be controlled to achieve a desired level of dilution selected based upon an expected concentration range of the analyte-being-characterized in the sample. As appreciated by those of ordinary skill in the art, if a mass spectrometer is being used to characterize the concentration of an analyte at the parts-per-trillion range (ppt), one would now want to use a spike having a concentration in the parts-per-trillion range (ppt). However, as noted by the Applicants, most spike solutions become unstable at concentrations of less than the ppm range. Applicants have thus cleverly provided an automated system that can, on-the-fly, dilute a relatively-concentrated-but-stable spike to the appropriate diluted concentration.

The prior art patent (USP 5,414,259) and application (Ser. No. 09/015,469) (collectively, the "SIDMS references") formerly incorporated by reference in this application stand in sharp contrast. The SIDMS references address a problem inherent with inductively coupled plasma ionization: such ionization is relatively harsh and will destroy species information as described previously. Thus, the SIDMS references disclose a "speciated" IDMS technique involving physical separation so that the species information is not destroyed. But note that the present invention involves the use of API such that the species information is typically not destroyed. Thus, none of the physical separation steps and complications disclosed in the SIDMS references need be practiced by the present invention. Even more fundamentally, the present invention does not even require the IDMS technique to form its ratio measurements, let alone practice the specialized analysis denoted as "SIDMS" in the SIDMS reference. Thus, it was a drafting error by the applicants to state beginning on page 2, line 13 that "in a preferred

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embodiment the system of the invention uses a modified form of Isotope Dilution Mass Spectrometry (IDMS) known to the inventors as Speciated Isotope Dilution Mass Spectrometry (SIDMS)." It is now applicants' right (and duty) to correct this misstatement by deleting it. The same analysis and reasoning applies to the other specification amendments objected to as introducing "new matter."

Applicants respectfully traverse the rejection of claims 114, 116-117, and 124 with respect to the dilution range limitations. Consider Figure 6, which illustrates an embodiment of the spike dilution apparatus claimed, for example, in claim 119. Note the arrows showing the movement of syringes 619, 643, 645, 647, and 663. As stated on page 9, lines 15-23:

> The mechanism for providing portions of the solution may comprise a syringe connected by intermediate conduit to the isotope reservoir below a surface of the mixture in the reservoir, such that withdrawing a plunger of the syringe by a precise distance draws a precise volume of the mixture in the isotope reservoir into the syringe, and the syringe may comprise a plunger driven by the control and management system through a precision translation mechanism, enabling precision volume control. Plunger translation may be varied, and may be through use of a precision stepper motor. (emphasis added)

To make this variable dilution feature more clear, applicants have emphasized the statement "plunger translation may be varied, and may be through the use of a precision stepper motor." In other words, the amount of fluid drawn into a particular syringe is not "all or nothing." Instead, it is virtually an infinite range, limited only by the particular resolution provided by a given "precision stepper motor." For this reason, applicants noted on page 32, lines 5-7 that "a description of operation in all instances would be highly redundant, so only a smaller description is given here" with respect to the 33 ppb spike preparation described therein. Applicants respectfully submit the following: suppose a user desired a 15 ppb spike? Would the dilution apparatus module shown in Figure 6 then have to discarded and replaced with another module? The answer is, of course, "no, the control of the stepper motors would be adjusted appropriately." That is the beauty of the module shown in Figure 6. Applicants note that the 30:1 dilution range for each syringed described with respect to Figure 6 is just an example. The actual range

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would depend upon the total volume of each syringe and is entirely arbitrary. However, it can be easily seen that the range for each syringe in Figure 6 is 30:1. Thus, 1 ppm may be diluted to a maximum of 30 times to produce 33 pbb, which in turn may be diluted 30 times to produce 1 ppb, and so on. In any case, applicants note that "written support" is defined by what one of ordinary skill in the art would ascertain from reviewing the specification and the figures. Accordingly, abundant written support exists for the limitation in claim 114 of "wherein the range of possible dilutions for each dilution sub-module is from 1 to approximately 30." Similarly, support for claim 116 is provided by the first paragraph on page 32, in which the applicants described the varying of the "rate of plunger travel" to assist in the dilution process. Support for claim 117 is provided by original claim 9. In that regard, the paragraph beginning on page 32, line 8 had been amended as described in the previous response. Finally, claim 124 is supported in an analogous fashion as described with respect to claim 114.

Claim 109 has been amended to include "a spike reservoir" to address the "essential element" rejection of claims 109-117.

Claim 109 has been amended to remove "the components" limitation to address the lack of antecedent basis. However, applicants respectfully traverse the indefiniteness rejection with respect to the limitation of "configurable to." As an initial matter, applicants note that the functional limitation of being "configurable to (do something)" is a commonplace claim limitation – a search on the USPTO database shows thousands of issued patents with this limitation. The need for such a limitation is plain from an examination of, for example, Figure 6. Note the numerous valves and syringes. They are configurable in many different configurations. It depends upon the control signals they receive as to what particular configuration is achieved. Thus, the limitation in claim 114 of a "spike dilution apparatus configurable to dilute a spike from the spike reservoir having a first concentration to produce a processed spike having a diluted second concentration" is entirely appropriate. Yes, the dilution apparatus does not "always have that configuration" as objected to in the office action: it depends upon the control from the claimed controller whether it does or not. The key is that it has this configurability. If it is an invention to provide that configurability, an applicant is perfectly entitled to claim it. Accordingly, the "configurable to" limitations of claims 109, 110, 113, 116, and

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118 are definite. Furthermore, consider the example set forth in MPEP 2173.05(g), in which the functional limitation: "whereby said housing may be slidably positioned" was deemed definite and proper. That same limitation could be recast as "whereby said housing is configurable to be slidably positioned." In that regard, the use of "configurable to" has been sanctioned as proper in the thousands of issued patents referred to previously.

Claims 115, 119, and 124 are definite by analogy to the example claim previously quoted from MPEP 2173.05(g).

Applicants respectfully traverse the indefiniteness rejection of claim 119-124 with respect to a missing step of "that the spike concentration is about the same concentration as the analyte in the sample." Indeed, Applicants note that such a rejection would be justified if

they had stated something to the effect of "in all embodiments, it is critical that the spike concentration be the same concentration as the analyte." But that is not the case – it is simply helpful to the analysis for such a concentration to be achieved. It is not critical or essential, however. In that regard, applicants note that the quotation from page 30, lines 22-27 cited to support this rejection starts off with the phrase: "it is necessary in embodiments of the invention that the relative concentration of the spike..." (emphasis added). The sole support given for this rejection thus contradicts the criticality or essentialness of this "missing step." Applicants respectfully submit that they are not required to limit their claims unnecessarily in this fashion.

Applicants respectfully traverse the obviousness rejections of claims 109-124. The "base" references of these rejections will be discussed first, followed by the "in view of" refererences.

The Base References:

The Marchante-Gayon reference merely discloses the use of a manually-operated ICP-MS apparatus. Applicants readily admit such an apparatus is abundantly in the prior art. Marchante-Gayon provides no teaching or suggestion for a single limitation of claim 109.

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The Viczian reference adds nothing further: it too discloses the use of a manually-operated ICP-MS instrument. Viczian thus provides no teaching or suggestion for a single limitation of claim 109.

Finally, the Rottmann reference also discloses the use of a manually-operated ICP-MS apparatus. Applicants again readily admit such an apparatus is abundantly in the prior art. Moreover, Applicants note that the "on-line" characterization of the Rottmann apparatus is misleading in that the "on-line" feature merely refers to the premixed spike being continuously pumped to one leg of a tee mixer where it is mixed with HPLC effluent and then sent to the ICP-MS (see, e.g., Figure 1 of this reference). Such an "on-line" feature is a far cry from Applicants' fully-automated apparatus that may be run without the need for human intervention. Thus, the Rottmann reference provides no teaching or suggestion for a single limitation of claim 109.

Given that the base references provides no teaching or suggestions for any limitations of claim 109, let alone their inventive combination as set forth above, what do the "in view of" references provide with respect to these missing teachings?

Applicants immediately note that the Koster reference (USP 6,730,517) is merely directed to the use of an MALDI-TOF mass spectrometer. As known in the art, the MALDI-TOF technique is qualitative, not quantitative. Thus, all the Koster mass spec does is provide an indication whether a given genotype is present or not (see, e.g., Col. 19, lines 35-41). In that regard, Koster makes absolutely no teaching or suggestion for the "spike dilution apparatus" apparatus of claim 109. Instead, as known in the MALDI-TOF arts, a sample is mixed with a matrix and then dried to prepare it for analysis (see, e.g., Col. 17, line 60 through Col. 18, line 44). Furthermore, Koster makes no teaching or suggestion for the advantageous API stage of claim 109. Finally, Koster makes no teaching or suggestion for the limitations of "a mass spectrometer configurable to process the ions by ratio determination; and a control system adapted to automatically configure the spike dilution apparatus, the mixer, and the API such the sample is automatically mixed with the processed spike, ionized, and processed by the mass spectrometer, the control system being further configured to use the ratio measured by the mass spectrometer to characterize the concentration of the at least one

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analyte in the extracted sample." In sum, Koster is deficient on each and every limitation of claim 109.

The sole teaching of the Maxwell reference is an "automated spike preparation system." The abstract does not disclose that this spike preparation system is "configurable to dilute a spike from the spike reservoir having a first concentration to produce a processed spike having a diluted second concentration" as set forth for the spike dilution apparatus of claim 109. Instead, all that is disclosed for the Maxwell spike preparation system is that the spikes have "duplicate net wts." As such, the Maxwell spikes are not produced at an arbitrary diluted second concentration as follows from the functional limitation of "configurable to dilute a spike ... having a first concentration to produce a processed spike having a diluted second concentration" in claim 109. Maxwell is entirely silent regarding the remaining elements of claim 109. Thus, just like Koster, Maxwell is deficient with respect to every limitation of claim 109.

The Multala reference merely discloses a mass spectrometry system in which samples from various points in a distillation column are fed continuously into a mass spectrometer. Because no spiking is performed or suggested, the Multala apparatus could never characterize the concentration of the at least one analyte as performed by the system recited in claim 109. Accordingly, Mutlala provides no teaching or suggestion for a single limitation of claim 109.

Finally, the Durealt reference merely discloses a "fluidic module" configured to dilute samples. It is entirely silent with respect to the disclosure of any mass spectrometry let alone the automated ICP-MS system recited in claim 109. Accordingly, Durealt reference provides no teaching or suggestion for a single limitation of claim 109.

Applicants note that claim 109 is not simply claiming "an automated mass spectrometer." There are six separate limitations in claim 109, all of which must be considered in forming an obviousness rejection. Based upon the art of record, such a rejection can only be grounded in sheer hindsight. Accordingly, claim 109 and its dependent claims 110 through 118 are patentable over the art of record. Claims 119 and

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its dependent claims 120 through 124 are patentable over the art of record analogously as discussed with respect to claim 109.

## CONCLUSION

For the foregoing reasons, Applicant respectfully submits that pending claims 109 - 124 are in condition for allowance.

If there are any questions regarding any aspect of the application, please call the undersigned at 949-752-7040.

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